10. (Twice Amended) The polynucleotide of Claim 9, which:
    a) encodes a mature polypeptide of SEQ ID NO: 2 or 4, that lacks an N terminal leader sequence;
    b) comprises a [the] mature polypeptide coding portion of SEQ ID NO: 1 or 3, that does not encode an N terminal leader sequence;
    c) comprises a [the] extracellular domain of SEQ ID NO: 2 or 4; or
    d) comprises a [the] intracellular domain of SEQ ID NO: 2 or 4.

11. (Twice Amended) A recombinant expression or replicating vector comprising [said] the isolated or recombinant polynucleotide of Claim 9.

12. (Twice Amended) A kit comprising
    a) [said] the isolated or recombinant polynucleotide of Claim 9; and
    b) instructions for use or disposal of reagents in said kit.

17. (Twice Amended) A method of producing a polypeptide, comprising expressing [said] the recombinant expression or replication vector of Claim 11 in a host cell and isolating said polypeptide, thereby producing said polypeptide.

18. (Twice Amended) A cell comprising [said] the recombinant expression or replication vector of Claim 11.

19. (Reiterated) A recombinant or isolated polynucleotide of Claim 9, that encodes at least 15 contiguous amino acid residues of SEQ ID NO: 4.

20. (Twice Amended) The isolated or recombinant polynucleotide of Claim 19, wherein said contiguous amino residues number at least 17.

23. (Amended) The isolated or recombinant polynucleotide of Claim 9, wherein said hybridization occurs over the entire open reading frame of SEQ ID NO: 1.

24. (Amended) The isolated or recombinant polynucleotide of Claim 9, wherein said polynucleotide is a variant due to the degeneracy of the genetic code[:
   a) encodes a polypeptide with a natural sequence of the mature coding portion of SEQ ID NO: 2;
   b) encodes a polypeptide with a natural sequence of the mature coding portion of SEQ ID NO: 4;
   c) is isolated from nature;
   d) encodes a polypeptide comprising 5 or fewer conservative substitutions from a natural sequence of SEQ ID NO: 2; or
   e) encodes a polypeptide comprising 5 or fewer conservative substitutions from a natural sequence of SEQ ID NO: 4].

25. (Amended) The isolated or recombinant polynucleotide of Claim 9, wherein said wash conditions are
   a) at least 60[5]° C;
   b) less than 150 mM salt; or
   c) both a) and b).

26. (Amended) A method of producing a polynucleotide duplex comprising contacting [said] the isolated or recombinant polynucleotide of Claim 9 with a second polynucleotide for a time sufficient to produce said duplex under stringent wash conditions of at least 60° C and less than 250[0] mM salt; thereby forming said duplex.

27. (Amended) The isolated or recombinant polynucleotide of Claim 9, which is:
   a) is attached to a solid substrate;
   b) is detectably labeled;
   c) is in a sterile composition;
   d) encodes an antigenic polypeptide having at least 12 amino acid residues; or
   e) is synthetically produced.

28. (Amended) The isolated or recombinant polynucleotide of Claim 19, which comprises:
   a) at least 57 contiguous nucleotides from the mature protein coding portion of SEQ ID NO: 1 or 3 that lacks an N terminal leader sequence; or
   b) is a variant due to the degeneracy of the genetic code.

29. (Amended) The isolated or recombinant polynucleotide of Claim 27, wherein:
    a) said contiguous amino acid residues number at least 21; or
    b) said contiguous nucleotides are from nucleotides 26-165 or nucleotides 191-241 of SEQ ID NO: 4.

30. (Amended) An isolated or recombinant polynucleotide encoding a polypeptide that:
    a) has a conservative amino acid substitution of a mature polypeptide of SEQ ID NO: 2 or 4 that lacks an N terminal leader sequence;
    b) is a natural allelic variant of the mature native polypeptide of SEQ ID NO: 2 or 4 that lacks an N terminal leader sequence; or
    c) is a species variant of the mature native polypeptide of SEQ ID NO: 2 or 4 that lacks an N terminal leader sequence.

31. (Amended) The isolated or recombinant polynucleotide of Claim 30, which is from SEQ ID NO: 4.

32. (Amended) The isolated or recombinant polynucleotide of Claim 30, comprising:
    a) nucleotides 124 to 751 of SEQ ID NO: 1; or
    b) nucleotides 54 to 723 of SEQ ID NO: 3.

33. (Amended) A method of producing a polynucleotide duplex comprising contacting [said] the isolated or recombinant polynucleotide of Claim 30 with a second polynucleotide for a time sufficient to produce said duplex under stringent wash conditions of at least 60° C and less than 200 mM salt; thereby forming said duplex.

34. (Amended) A recombinant expression or replicating vector comprising [said] the isolated or recombinant polynucleotide of Claim 30.

35. (Amended) A cell comprising [said] the recombinant expression or replication vector of Claim 34.

36. (Amended) A method of producing an antigenic polypeptide, comprising expressing [said] the recombinant expression or replication vector of Claim 34 in a host cell and isolating said antigenic polypeptide, thereby producing said antigenic polypeptide.

37. (Amended) A recombinant or isolated polynucleotide that [selectively] hybridizes to the open reading frame of SEQ ID NO: 1 or 3 under stringent hybridization and wash conditions of at least 55[0]°C, a salt concentration of less than 250[0] mM, and 50% formamide.

38. (Amended) The polynucleotide of Claim 37:
a) wherein said wash conditions are at least 7[6]0°C;
b) that encodes an antigenic polypeptide;
c) comprises at least 36 contiguous nucleotides of the mature coding portion of SEQ ID NO: 1 or 3 that does not encode an N terminal leader sequence; or
d) comprises at least 20 contiguous amino acids of the mature coding of SEQ ID NO: 4 that lacks an N terminal leader sequence.

39. (Amended) The polynucleotide of Claim 37, further encoding:
a) [a two-fold or] less than three conservative amino acid substitutions of a mature polypeptide of SEQ ID NO: 2 or 4 that lacks an N terminal leader sequence;
b) a natural allelic variant of the native polypeptide of SEQ ID NO: 2 or 4; or
c) a species variant of the native polypeptide of SEQ ID NO: 2 or 4.

40. (Amended) A recombinant expression or replicating vector comprising:
a) said polynucleotide of Claim 37; or
b) the mature polypeptide of SEQ ID NO: 4 that lacks an N terminal leader sequence.

41. (Amended) A cell comprising [said] the recombinant expression or replication vector of Claim 40.

42. (Amended) A method of producing an antigenic polypeptide, comprising expressing [said] the recombinant expression or replication vector of Claim 41 in a host cell and isolating said polypeptide, thereby producing said polypeptide.

43. (Amended) A method of producing a polynucleotide duplex comprising contacting said polynucleotide of Claim 37 with a second polynucleotide for a time sufficient to produce said duplex under stringent wash conditions of at least 60° C and less than 250[0] mM salt; thereby forming said duplex.

Remarks

Applicants respectfully request examination and consideration of the newly amended claims and reconsideration of the application in view of the following.

Table of Contents

I. Status of The Application

Claims 1-43 are pending. Claims 9-12, 17-20, and 23-42 were acknowledged as allowable if the rejections under 35 U.S.C. §112, ¶1 and 2 were overcome. Applicants believe that the newly amended claims are fully supported and introduce no new matter. Attached, for the Examiner's convenience, is a listing of the revised claims. Applicants believe no new issues are raised in the presently pending claims and respectfully request examination of the newly amended claims.

II. The Invention

The present invention is based, in part, upon the discovery of a family of polypeptides that appear to act as a costimulator of T cell activation. In particular, the invention provides mammalian, e.g., rodent and primate, polynucleotide sequences that are expressed in the thymus, and are induced on T cells and spleen cells following activation.

III. The Non-Art Rejections and Objections Rejections

Section 112 First Paragraph Rejections

Claims 9-12, 17-20, and 23-43 were rejected under 35 U.S.C. §112, ¶1. (Nos. 6 and 7). Applicants traverse the rejections.

Specifically, the Office Action alleges that the hybridization limitations of claims 9, 25-26, 30, 32, 33, 37, and 43 are not supported in the specification, however, the Examiner suggested the rejections could be overcome by reciting the hybridization conditions listed at page 37 of the specification (see, the last sentence of No. 7 of Paper No. 12). Applicants thank the Examiner for the helpful suggestion and have adopted the hybridization conditions

described in the specification. Accordingly, Applicants respectfully request withdrawal of the rejections.

The Office Action also alleges that the phrases "mature polypeptide" and "mature coding portion" of Claims 10, 30, and 40 are not supported in the specification.

To clarify, the phrase "mature polypeptide" refers to a polypeptide that has undergone processing to remove a leader sequence, and the phrase "mature coding portion" refers to a polynucleotide sequence that does not encode the leader sequence of such a polypeptide. Therefore, Applicants added the phrase, "that lacks an N-terminal leader sequence" to the claims at issue to specify what the term "mature" is defining. Support is provided e.g., at page 19, lines 6-7; and at page 20, lines 25-36. There Applicants' specification teaches that the polypeptides of the invention have an N-terminal leader sequence which is processed, e.g., typically by cleaving, before the "mature" polypeptide is created. The term "mature polypeptide" is a phrase that is commonly used in the art to refer to such processing. As evidence of this belief, Applicants include herein (Appendix B) a copy from a standard textbook in the art (Alberts et al. (ed.; 1989) Molecular Biology of the Cell 2nd ed., Garland Pub., N.Y., N.Y.) illustrating how cleavage of a leader sequence results in a "mature" protein. Accordingly, Applicants respectfully request withdrawal of the rejections.

The Office Action also alleged that the polynucleotide residues recited in Claim 32 were not described in the specification and thus were rejected as new matter. Applicants traverse the rejection. This rejection is related to the above rejection, since these polynucleotide sequences refers to the fragment of SEQ ID NO: 1 or 3 that encodes respectively the N-terminal leader sequence of the corresponding polypeptides of SEQ ID NO: 2 or 4. The leader sequences are described in the specification at page 20, lines 25-36 as amino acid residues, however, the residues in Claim 32 are merely the corresponding polynucleotide fragments encoding these amino residues. Therefore, they are disclosed in the specification as it describes the relationship of the polynucleotide sequence with its cognate amino acid sequence. Therefore, the Claim does not contain new matter and, should be withdrawn.

Claim 24 was rejected as the specification allegedly did not provide enablement for all the variants of the claim. Applicants traverse the rejection, however, to advance prosecution Applicants have amended the claim to recite that the only polynucleotide claimed is one which is a result of the degeneracy of the genetic code. Support can be found

in the specification at page 7, lines 10-36. Accordingly, Applicants respectfully request withdrawal of the rejection.

Section 112 Second Paragraph Rejections

Claims 9-12, 17-18, and 20-42 were rejected under 35 U.S.C. §112, ¶2, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter of the invention (No. 12). While Applicants traverse, the rejections should now be moot due to the present amendments which Applicants believe provide a cure. Accordingly, Applicants respectfully request withdrawal of the rejections. Specifically:

- Claims 19 and 20 were alleged still indefinite under 35 U.S.C. §112, ¶2, based on Applicants' amendment of 18-MAR-99 (Paper No. 11) over use of the phrase "at least about." (Nos. 4 and 5). Applicants respectfully traverse the rejection as the phrase was previously amended to recite "at least." Accordingly, the rejections are moot in view of the former amendment of the claims in Paper No. 11.

- Claims 9 and 37 were alleged indefinite for the phrase "selectively hybridizes." (No. 13). Applicants have removed the term "selectively" accordingly, no indefinitness should still exist.

- Claims 10, 30, 38(c), 38(d), and 40 were alleged indefinite for the phrase "mature polypeptide." (Nos. 14 and 21). To clarify that the phrase "mature polypeptide" refers to a polypeptide that has undergone processing to remove a leader sequence, Applicants have added the phrase, "that lacks an N-terminal leader sequence" to the claims. Support is provided e.g., at page 19, lines 6-7; at page 20, lines 25-36; and as described above.

- Claims 10-12, 17, 18, 20-29, 31-36, and 41-42, were alleged indefinite for lack of antecedent basis. (Nos. 15-18). Applicants thank the Examiner for the helpful suggestions and have adopted language similar to that suggested.

- Claim 31 was alleged indefinite over recitation of the phrase "from SEQ ID NO:4" since it appears a polynucleotide sequence was suggested. (No. 19). Applicants thank the Examiner for the helpful suggestions and have adopted language reciting, "SEQ ID NO:3."

- Claim 36 was alleged indefinite over recitation of the phrase "said polypeptide." (No. 20). Applicants thank the Examiner for the helpful suggestion and have adopted the suggested language reciting, "said antigenic polypeptide."

- Claim 39 was alleged indefinite over use of the phrase "two-fold or less conservative amino acid substitution" as it was unclear how a substitution could be a two-fold substitution. (No. 22). Applicants desired to indicate that the mature polypeptide had one or two conservative amino acid substitutions therefore, to clarify the claim, the language was changed to recite, "less than three conservative amino acid substitutions."

- Claims 17, 36, and 42 were alleged indefinite for lacking essential conditions. (No. 23). Specifically, the Examiner suggested adding the conditions of a host cell and obtaining or isolating the polypeptide from the culture. Applicants thank the Examiner for the helpful suggestion and have adopted language similar to that suggested.

For all of the reasons given above, Applicants believe that Claims 9-12, 17-18, and 20-42 should now longer be rejected under 35 U.S.C. §112, ¶2. Accordingly, Applicants respectfully request withdrawal of all the Section 112, paragraph two rejections.

Conclusion

Applicants maintain that presently amended claims (Claims 9-12, 17-43; Appendix A) clearly and patentably define the invention. Accordingly, Applicants respectfully request reconsideration and passage of the pending claims to allowance at the earliest possible convenience.

Applicants believe the present amendments and response to the objections and/or rejections raised in the 07JUN-1999 Office Action (Paper No. 12) represent a complete, timely, and good faith response to all the issues raised therein. Should the Examiner deem that allowance is not appropriate, Applicants respectfully request an interview be granted